Saudi Pharmaceutical Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

Original article

Comparison of the safety information on drug labels in three developed countries: The USA, UK and Canada

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ARTICLE INFO

Article history:
Received 17 April 2017
Accepted 9 July 2017
Available online xxxx

Keywords:
Drug labelling
Drug safety
Boxed warnings
Contraindications

ABSTRACT

The safety information on drug labels of a company marketing the same drugs in different countries is sometimes different. The aim of the present study is to understand the differences in the volume and content of safety information on the drug labels from the same manufacturers in three developed countries: the United States of America (USA), the United Kingdom (UK) and Canada. This study involved the calculation of the proportion of total safety information (PSI) and of contraindications (PCI) in comparison to all information on the label and the percentage of boxed warnings (PBW) among the 100 labels studied from each country. The PSI on the labels of different countries is different with USA labels bearing lesser value PSI and UK labels bearing higher value PSI. The qualitative information provided on these drug labels from each country in 'contraindications' sections, 'boxed/serious warnings' and 'overdosage' sections presented differences in the information provided on most of the labels. We have found distinct differences between the safety information available on drug labels in terms of volume and content. We conclude that the safety information for the same products should be standardised across all countries.

1. Introduction

Drug labels are the essential means of communication of important information on drug safety to healthcare professionals and patients (Davis et al., 2006). These labels are the primary source of information from manufacturers to healthcare professionals (Duke et al., 2011). Drug labels are prepared by the manufacturers and are reviewed by the Food and Drug Administration (FDA) or a similar body in a particular country (Cooper, 1986). Guidelines for the structure and content of drug labels are generally given by the regulatory authorities of the respective countries. In the United States of America (USA), the FDA issues guidance for requirements on content and format of labelling. In United Kingdom (UK), Summaries of Product Characteristics (SPCs) are checked and approved by the Medicines and Healthcare Products Regulatory Agency (MHRA), and in Canada, Health Canada looks after the information on drug labels (DailyMed, 2016; Electronics Medical Compendium, 2016; Health Canada, 2016). Generally, drug labels contain useful information about the therapeutic indications, dosing, drug interactions, adverse drug effects and the drug's toxicity details (Requirements on Content and Format of Labelling for Human Prescription Drug and Biological Products. Final Rule, 2006). The labels are available on the websites of the regulatory authorities and are updated regularly in the light of important new information on the specific drug (Raymond, 2000). Many labels contain comprehensive lists of adverse events. However, exhaustive lists of adverse events result in the poor readability of the labels, which consequently may result in overlooking serious risks and warnings (Duke et al., 2011). Regulatory authorities continuously monitor drug labels to improve the readability and understandability of the labels and as well as ensure any new drug safety information is listed (Blank, 2015; King et al., 2016; Kircik et al., 2016). Studies have also focused on improving the readability of the labels (Abedtash and Duke, 2015).

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Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jsps.2017.07.006
1319-0164/

Please cite this article in press as: Alshammari, T.M., et al. Comparison of the safety information on drug labels in three developed countries: The USA, UK and Canada. Saudi Pharmaceutical Journal (2017), http://dx.doi.org/10.1016/j.jsps.2017.07.006

We would expect that the information on drug labels in different countries for the same drug would be similar as the regulatory authorities evaluate the same scientific data (Shimazawa and Ikeda, 2013a). This expectation is high, particularly when the drug is supplied by the same manufacturer in different countries. In this study, we assessed the safety information on the labels supplied by the same company in different countries. The aim of the present study is to investigate any differences in safety information in developed countries and to provide an evidence base for better drug safety communication.

2. Methods

2.1. Data sources

This study was a cross-sectional study conducted in the period between January and March 2016. The present study included drugs approved in the USA, the UK and Canada. The drug labels were identified from the DailyMed, electronics Medical Compendium (eMC) and Health Canada for the USA, the UK and Canada, respectively (DailyMed, 2016; Electronics Medical Compendium, 2016; Health Canada, 2016). Structured product labels, summaries of product characteristics and product monographs were used from the above said websites in the USA, the UK and Canada, respectively. From these labels, we randomly identified labels that are prepared by the same company in all three countries by manual search. Three hundred such labels were used in our study, 100 from each country. These drug labels were also analysed qualitatively for the information provided in the 'contraindications' sections, 'boxed/serious warnings' and 'overdose' sections. Differences in information within these sections were identified manually and listed in Tables.

2.2. Variable definitions, evaluation and analysis

We performed a direct comparison of the proportion of all information given to safety information (PSI), and contraindications (PCI) in the three countries. The PSI was calculated by dividing the total number of safety words with the total number of label words. The PCI was calculated by dividing the number of words on contraindications to the total number of words on the label. Similarly, the percentage of boxed warnings (PBW, in the USA and Canada) was calculated by dividing the number of labels with boxed warnings and the total number of labels. The total number of safety words was calculated based on the sections listed in Table 1 from each country. Boxed warnings or serious warnings were identified by manual search on USA drug labels or Canadian drug labels, which we included in calculating safety words for that particular country. In regard to the UK, there are no warnings given in a special box for any drug on the label from the drugs we screened in our study. However, on some labels there is a box on serious adverse effects; for example, on the label of thalidomide, we can find a boxed warning for teratogenic effects (Thalidomide Drug Label in UK, 2016). The label information was analysed after grouping the drugs according to Anatomical Therapeutic Chemical (ATC) classification codes (Table 2).

2.3. Qualitative comparison of the product label information

There is a possibility that the volume of text is different, but the information conveyed is the same. To understand the differences in the information provided across the three countries, the actual information that is illustrated in the contraindications sections, serious/boxed warnings and overdosage sections was read, and information that was different was identified and tabulated.

2.4. Statistical analysis

Descriptive statistics were performed on the data obtained. Data were presented as the mean and standard deviation (SD). One way analysis of variance (One way ANOVA) was performed to find out the differences between groups followed by Scheffe's post hoc test to determine which means were different with a level of significance set at $p < 0.05$. Data were analysed using Statistical Analysis Software (SAS version 9.3).

3. Results and discussion

A total of 100 drug labels in each country were counted for the total number of words on the label. The total number of label words on the Canadian labels (14843 [7018] (Average [standard deviation])) was higher than the number of USA (10724 [6406]) and UK (5637 [3379]) label words with a p value < 0.05. The total number of safety words was also higher on Canadian labels (6235 [3486]) when compared to the USA (3873 [2616]) and the UK (2757 [1674]) label safety words with a p value < 0.05. The number of words on the label indicating contraindications was higher in Canada (83 [73]) than for the UK (49 [47]) with a p value < 0.05. Overall, the number of words on the label, safety information words and contraindication words were higher in Canada.

We have noticed differences in the amount of information provided on the drug labels although the labels were prepared by the same manufacturers in the USA, the UK and Canada (Online only Tables S1–S6). The USA and Canadian labels contained almost double the volume of information contained in the UK labels. Although the regulatory authorities reviewed the labels by the same manufacturer, the information on the USA and Canadian labels is more voluminous most likely due to the guidelines set by these authorities for the preparation of drug labels (Best

Table 1
Drug label information for analysis.

Categories for analysis	Drug label sections		
	USA	UK	Canada
Safety information	Boxed warnings	4.3 Contraindications	Serious warnings
	4. Contraindications	4.4 Special warnings and precautions	Contraindications
	5. Warnings and precautions	4.5 Interaction with other medicinal products	Warnings and precautions
	6. Adverse reactions	4.6 Pregnancy and lactation	Adverse reactions
	7. Drug interactions	4.7 Effects on ability to drive and use machines	Drug interactions
	8. Use in specific populations	4.8 Undesirable effects	Over dosage
	10. Over dosage	4.9 Overdose	Toxicology
	13. Non clinical toxicology	5.3 Preclinical safety data	
Contraindications	4. Contraindications	4.3 Contraindications	Contraindications
Serious warnings	Boxed warnings	Not applicable	Serious warnings and precautions

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